REMARKS

Reconsideration of the present application in view of the present amendments and the following remarks is respectfully requested. In response to a Restriction Requirement, Applicants elected Group I (claims 1, 5-7) for examination, to which the PTO has re-joined claims 3 and 4. Claims 1 and 3-7 therefore are currently under examination. Applicants hereby cancel non-elected claims 2 and 8-24 without prejudice to further prosecution of this subject matter in a related divisional, continuation, or continuation-in-part application. The Examiner also withdrew the requirement to elect a single sequence; therefore, SEQ ID NOs:1, 3, and 5 will be examined together. Applicants have amended claims 1, 3, 5, and 6 and have added new claims 25-31 to define more clearly the subject matter that Applicants regard as their invention. Support for the amended claims may be found in the specification, for example, at page 4, line 27 through page 5, line 10; page 11, lines 10-15; page 20, lines 4-10; page 21, lines 10-22; page 22, lines 15-27; page 28, lines 10-18; page 29, lines 10-27; page 38, lines 4-10; page 65, line 9 through page 66, line 4. No new subject matter has been added.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (ENABLEMENT)

The PTO rejects claims 1 and 3-7 under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the PTO asserts that the scope of the claims is not commensurate with the disclosure of the specification. The PTO alleges that the specification does not teach a specific biological activity of a polypeptide encoded by SEQ ID NO:1, 3, or 5 such that a skilled artisan would be able to predict whether a nucleic acid encodes a matrix metalloproteinase on the basis of its nucleotide sequence or its ability to hybridize to any of SEQ ID NO:1, 3, or 5. The PTO further alleges that the specification does not enable any uses for the claimed sequences other than for nonspecific uses such as expressing proteins or making probes and primers to detect the claimed sequences.

Applicants respectfully traverse this rejection and submit that as disclosed in the present specification and recited in the instant claims, Applicants fully enabled the claimed invention at the time the instant Application was filed. Applicants' invention is directed in

pertinent part to an isolated nucleic acid molecule consisting of a nucleotide sequence set forth in SEQ ID NO:1, a nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO:3 or SEQ ID NO:5, or the complementary sequences thereof; and to a nucleic acid molecule that is at least 85% identical to the nucleotide sequence set forth in SEQ ID NO:5, wherein the nucleic acid molecule encodes a MMP-25 polypeptide that exhibits catalytic activity that is the same as that of a wild-type MMP-25 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:6, and to related compositions and methods. In another embodiment, the invention is directed to a method of identifying a nucleic acid molecule encoding all or a part of a MMP-25 polypeptide, comprising hybridizing a nucleic acid molecule sample to an oligonucleotide encoding a peptide that consists of an amino acid sequence consisting of amino acids at positions 1-61, 98-111, or 161-170 of SEQ ID NO:6; and identifying a sequence in the nucleic acid sample that hybridizes to the oligonucleotide under high stringency conditions.

Applicants submit that the instant specification provides explicit guidance enabling a person skilled in the art to make and use the nucleic acid molecules and related compositions and methods as recited in the claims, readily and without undue experimentation. As taught in the present specification, the claimed nucleic acid molecules encode a novel full-length matrix metalloproteinase polypeptide (MMP-25) and related splice variants and fragments. The specification discloses that the claimed nucleic acid molecule comprising the sequence set forth in SEQ ID NO:5 encodes a full-length MMP-25 polypeptide (SEQ ID NO:6) that contains conserved motifs present in other known matrix metalloproteinases and known to be important for activity and function of the metalloproteinases. The motifs include a first zinc binding domain (SEQ ID NO:17), a second zinc binding domain that also binds calcium (zinc/calcium binding domain) (SEQ ID NO:37), and a cysteine-switch motif (SEQ ID NO:18) located within the pro-peptide (*see, e.g.,* page 2, lines 5-19; page 14, line 19 through page 15, line 2; page 16, lines 17-22; Figure 3). The specification teaches that the nucleotide sequence encoding the MMP-25 polypeptide was obtained by probing a mammary gland cDNA library with a set of primers derived from SEQ ID NO:1, which consists of a polynucleotide fragment of SEQ ID NO:5 (*see, e.g.,* page 15, line 19 through page 17, line 4; page 16, lines 6-16; Example 1; *see also* page 2, lines 5-19). The specification also teaches that the claimed nucleic acid

molecule comprising the sequence set forth in SEQ ID NO:3 encodes a MMP-25 splice variant (SEQ ID NO:4) that contains a zinc binding domain but lacks a zinc/calcium binding domain.

The instant specification also enables a person skilled in the art to make and use a nucleic acid molecule that is at least 85% identical to the nucleotide sequence set forth in SEQ ID NO:5, wherein the nucleic acid molecule encodes a MMP-25 polypeptide that exhibits catalytic activity that is the same as that of a wild-type MMP-25 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:6. As taught in the instant specification, MMP-25 variants include polynucleotides that encode polypeptides that retain the structural and functional characteristics of an MMP-25 polypeptide encoded by the claimed polynucleotides (*see, e.g.*, page 21, lines 1-8). Such variants include allelic variants and synthetic sequences that contain conservative amino acid substitutions (*id.*). As discussed in more detail herein, the variants can be identified and functionally characterized, for example, by alignment methods, by the ability to bind specifically to an anti-MMP-25 antibody, and/or by the ability to degrade the same panel of protein substrates with the same relative catalytic activity as the wild-type MMP-25 (*see, e.g.*, page 21, lines 9-22; *see generally* page 19 line 27 through page 21, line 22).

The present specification teaches a skilled artisan how to identify an isolated polynucleotide that has a sequence encoding a MMP-25 polypeptide, or a variant thereof. For example, the sequence of the isolated polynucleotide may be compared to the disclosed MMP-25 polynucleotide sequence set forth in SEQ ID NO:5 using computer algorithms, such as ALIGN or BLAST, which are known in the art and described in the instant specification (*see, e.g.*, page 20, lines 11-28). A MMP-25 polynucleotide or variant thereof may also be identified by hybridization methods known in the art and described in the specification using an oligonucleotide probe that hybridizes to portions of SEQ ID NO:5 that are not common to other matrix metalloproteinases, wherein the oligonucleotide encodes a peptide consisting of an amino acid sequence set forth at positions 1-61, 98-111, or 161-170 of SEQ ID NO:6 (*see, e.g.*, at page 19, lines 19 through page 20, line 10; page 22, lines 15-22; page 23, lines 2-12; page 29, lines 10-27).

The novel MMP-25 polypeptide encoded by the claimed nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:5 is a newly discovered member of

the matrix metalloproteinase (MMP) family. Members of the MMP family are zinc-dependent endopeptidases that degrade proteins found, for example, in the extracellular matrix of animal tissue (*see, e.g.,* page 1, line 17 through page 4, line 14). The proteolytic activity of a MMP-25 polypeptide or a variant thereof can readily be determined by methods known in the art and disclosed in the specification. Most MMPs have overlapping substrate specificity and are able to degrade multiple substrates including collagens, laminins, gelatins, aggrecans, fibronectins, hyaluronidase treated versican, elastin, casein, vitronectin, entactin, fibrin, plasminogen, and proteoglycan linked proteins (*see, e.g.,* page 1, line 27 through page 2, line 4). An example of a proteolytic assay that may be performed without undue experimentation to determine proteolytic activity of a wild-type MMP-25 polypeptide or a variant thereof is a zymography method known in the art and described in detail in the specification, in which a protein such as gelatin is degraded in a polyacrylamide gel at the location in the gel to which the MMP has migrated (*see, e.g.,* page 60, line 25 through page 61, line 9; Example 5, page 65-66 and reference cited therein).

Applicants respectfully submit that given the teachings of the present specification and, *inter alia*, the level of skill in the art, performing any of the aforementioned procedures and assays would not amount to undue experimentation, but instead is merely a matter of permissible routine screening. (*In re Wands*, 858 F.2d 731, 736, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) ("Enablement is not precluded by the necessity for some experimentation such as routine screening.").

Applicants further submit, contrary to the assertion in the Action, that the instant specification enables a use for the claimed nucleic acid molecules. The novel MMP-25 polypeptide encoded by the claimed nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:5 is a newly discovered member of the matrix metalloproteinase family. As noted above, members of this family are zinc-dependent endopeptidases that degrade proteins found, for example, in the extracellular matrix of animal tissue (*see, e.g.,* page 1, line 17 through page 4, line 14). Control of MMP expression in a cell may affect one or more physiological processes such as angiogenesis, photoaging of skin, cancer, and hair growth (*id.*). With respect to modulating hair growth, Styczynski et al. (U.S. Patent No. 5,962,466) disclose that inhibition

of MMP activity in follicle cells leads to a reduction in hair growth (*see, e.g.,* present specification page 2, lines 27-29; page 60, lines 7-8) and that administering matrix metalloproteinase inhibitors in a hamster assay resulted in reduction of hair mass. Styczynski et al., however, do not disclose which matrix metalloproteinases were adversely affected by the inhibitors in the hamster assay described therein, nor do Styczynski et al. show which matrix metalloproteinases are expressed in skin cells (*see* Styczynski, column 4; Table 1; *see* present specification, page 60, lines 7-15). In contrast, the present specification discloses that, unlike other known MMPs, the claimed nucleic acid molecules encoding a MMP-25 polypeptide are preferentially expressed in the inner root sheath layer of the hair follicle, particularly in the Henle layer, which contain cells involved in hair growth (*see, e.g.,* page 60, lines 7-20; page 64, lines 13-18; Figures 4 and 5). Thus, Applicants further submit, contrary to the assertion in the Action, that the present specification does not suggest that the ability of MMP-25 to modulate hair growth is "based solely on the degree of % identity exhibited by the protein to various other MMPs" (Action, page 6, lines 5-6). The instant specification further teaches a skilled artisan that the claimed MMP-25 nucleic acid molecules and encoded polypeptide may be used in assays to test inhibitors of MMP-25 activity, thus identifying inhibitors of hair growth (*see, e.g.,* page 58, line 1 through page 60, line 5; Example 5). Applicants therefore respectfully submit that the instant specification enables a person skilled in the art to make and use the claimed invention.

Applicants also respectfully disagree with the assertion in the Action that using the nucleic acid molecules of SEQ ID NOs:1, 3, and 5 to express proteins or to make probes and primers to detect these polynucleotides is a non-specific use. As discussed above and disclosed in the specification, SEQ ID NO:5 encodes a novel MMP-25 polypeptide and SEQ ID NO:3 encodes a splice variant of MMP-25, both of which are expressed at greater levels in skin cells compared with other MMPs. Furthermore, the MMP-25 nucleic acid fragment of SEQ ID NO:1 was used for identifying and selected the novel full-length sequence from a cDNA library (*see* Example 1). Unique MMP-25 nucleic acid fragments such as SEQ ID NO:1 and other fragments described in the specification and recited in the instant claims can be used for detecting expression of MMP-25 in other libraries, cells, and tissues. Such fragments are also useful for inhibiting expression of the MMP-25 polypeptide (*see, e.g.,* page 59, line 20 through page 60,

line 5). Control of MMP expression in various cell types is an important target for affecting physiological processes such as angiogenesis, hair growth, photoaging of the skin, and cancer (*see, e.g.,* page 2, lines 25-27).

Accordingly, Applicants submit that the specification enables a person skilled in the art to make and use the claimed invention, thus satisfying the requirements of 35 U.S.C. § 112, first paragraph. Applicants therefore respectfully request that the rejection of the claims be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The PTO rejects claims 1 and 3-7 under U.S.C. § 112, first paragraph, alleging that the claims are directed to subject matter that is not adequately described in the specification. In particular, the PTO alleges that the claims encompass a large genus of mutants, variants, and homologues of SEQ ID NOs:1, 3, and 5 that are not described by structure or function in the specification.

Applicants respectfully traverse this rejection and submit that as disclosed in the specification and recited in the instant claims, Applicants possessed the claimed invention at the time the Application was filed. As discussed above, Applicants' invention is directed in pertinent part to an isolated nucleic acid molecule consisting of a nucleotide sequence set forth in SEQ ID NO:1; to a nucleic acid molecule comprising a nucleotide sequence set forth in SEQ ID NO:3 or SEQ ID NO:5; to a nucleic acid molecule comprising a nucleotide sequence at least 85% identical to SEQ ID NO:5, wherein the nucleic acid molecule encodes a MMP-25 polypeptide that exhibits catalytic activity that is the same as that of a wild-type MMP-25 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:6; and to related compositions and methods.

Applicants submit that the instant specification describes sufficient relevant identifying characteristics of the claimed nucleic acid molecules. The specification discloses that MMP-25 is a new member of the matrix metalloproteinase family, the members of which are zinc-dependent endopeptidases that degrade proteins found, for example, in the extracellular matrix of animal tissue (*see, e.g.,* page 1, line 17 through page 4, line 14). The specification

describes a polynucleotide sequence (SEQ ID NO:5) that encodes a novel matrix metalloproteinase, MMP-25 (SEQ ID NO:6), which contains conserved consensus motifs that characterize this family of zinc dependent endopeptidases (*see, e.g.,* page 16, lines 17-22; Figure 3). The structure of the motifs, that is, the amino acid sequence, defines the function of these proteinases. The motifs include a first zinc binding domain that has a conserved peptide sequence (SEQ ID NO:17) in which three histidine residues form a complex with zinc to form a catalytic protease domain (*see, e.g.,* specification, page 2, lines 5-8; page 14, lines 19-24) (amino acid positions 215-234 of SEQ ID NO:6) and a second zinc binding domain that may also bind calcium (zinc/calcium binding domain) (SEQ ID NO:37) (amino acid positions 158-183 of SEQ ID NO:6) (*see also* Figure 3). Other conserved domains include a hemopexin domain and a cysteine-switch sequence that is located within the pro-peptide (SEQ ID NO:18; *see* amino acid positions 89-95 of SEQ ID NO:6; Figure 2 and Figure 3).

Also described in the instant specification are relevant identifying characteristics of the claimed nucleic acid molecule that is at least 85% identical to SEQ ID NO:5, which has the same catalytic activity as that of a wild-type MMP-25 polypeptide (*see, e.g.,* page 20, lines 8-10; page 21, lines 9-15). The encoded MMP-25 polypeptide variants preferably contain conservative amino acid substitutions such that the variants retain structural and function characteristics of wild-type MMP-25 (*see, e.g.,* page 21, lines 1-8; page 27, line 17 through page 28, line 7). A MMP-25 variant can be structurally characterized by its amino acid sequence, which includes the aforementioned conserved motifs that are described in the instant specification. A variant can be functionally characterized by its ability to bind to antibodies that are specific for wild-type MMP-25 or by its proteolytic activity (*see, e.g.,* page 21, 9-15; page 28, lines 17-18; *see also* pages 44-54 describing anti-MMP-25 antibodies). Most MMPs have overlapping substrate specificity and are able to degrade multiple substrates including collagens, laminins, gelatins, aggrecans, fibronectins, hyaluronidase treated versican, elastin, casein, vitronectin, entactin, fibrin, plasminogen, and proteoglycan linked proteins (*see, e.g.,* page 1, line 27 through page 2, line 4). Relative catalytic activity may be determined by methods known in the art and described in the specification, such as a zymography assay, in which a protein such as gelatin is degraded in a polyacrylamide gel at the location in the gel to which the MMP migrated

(*see, e.g.,* page 60, line 25 through page 61, line 9; Example 5, page 65-66 and reference cited therein). The present specification also discloses that, unlike other known MMPs, the claimed nucleic acid molecules encoding a MMP-25 polypeptide are preferentially expressed in the inner root sheath layer of the hair follicle, particularly in the Henle layer, which contain cells involved in hair growth (*see, e.g.,* page 60, lines 7-20; page 64, lines 13-18; Figures 4 and 5).

The specification also describes relevant identifying characteristics of a splice variant of MMP-25. The nucleotide sequence of an MMP-25 splice variant is set forth in SEQ ID NO:3 (*see, e.g.,* page 16, lines 23-29). This variant is characterized by a deletion of 43 amino acids found in the full-length MMP-25 polypeptide (SEQ ID NO:6), which comprises the region that corresponds to the zinc/calcium binding domain (*id.;* Figure 3; SEQ ID NO:4). This variant may represent a non-functional variant that acts as a dominant negative regulator of MMP activity (*see, e.g.,* page 56, line 7 through page 56, line 18). The specification also describes a MMP-25 nucleic acid fragment that consists of a nucleotide sequence set forth in SEQ ID NO:1 and describes that this nucleotide sequence is contained within SEQ ID NO:5 at positions 741-1573.

In view of the above remarks and the present amendments, Applicants respectfully submit that the presently claimed subject matter is sufficiently described by the specification to reasonably convey to a person skilled in the art that Applicants possessed the claimed invention at the time the Application was filed. Applicants therefore submit that the instant Application complies with the written description requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 102

The PTO rejects claims 1 and 3-7 under 35 U.S.C. § 102(e), alleging that the subject matter of the claims is anticipated by Robison (U.S. Patent No. 6,331,427). Specifically, the PTO asserts that Robison teaches a sequence (SEQ ID NO:78) that shares 99.4% identity with the complement of SEQ ID NO:1, 90.2% identity with the complement of SEQ ID NO:3, and 99.2% identity with the complement of SEQ ID NO:5. The PTO further asserts that Robison

teaches using the sequences disclosed therein for PCR and hybridization reactions and that Robison also teaches vectors and host cells comprising those polynucleotides.

Applicants respectfully traverse this rejection and submit that Robison cannot be regarded as novelty-destroying. Applicants submit herewith a Declaration under 37 C.F.R. § 1.131 in which the inventors declare that the invention of the presently claimed subject matter was complete prior to the effective filing date (March 26, 1999) of the Robison patent. Applicants therefore respectfully submit that the present claims meet the novelty requirements under 35 U.S.C. § 102 and request that the rejection be withdrawn.

The PTO rejects claim 1 under 35 U.S.C. § 102(b) as being anticipated by GenBank Accession No. AA424347. In particular, the PTO alleges that the document teaches a sequence that is identical to positions 1-411 of SEQ ID NO:1, to positions 653-1063 of SEQ ID NO:3, and to positions 741-1151 of SEQ ID NO:5. The PTO also asserts that AA424347 meets the limitations of claim 1b, allegedly because the claim is not limited to sequences that are 85% identical over the full length of the recited sequences.

Applicants respectfully traverse the grounds for this rejection and submit that AA424347 fails to anticipate the subject matter of the present claims. The cited document fails to teach or suggest an isolated nucleic acid molecule that consists of a nucleotide sequence as set forth in SEQ ID NO:1, and also fails to teach or suggest an isolated nucleic acid molecule that comprises a nucleotide sequence set forth in SEQ ID NO:3 or SEQ ID NO:5. AA424347 also fails to teach or suggest a nucleic acid molecule that comprises a nucleotide sequence that is at least 85% identical to the nucleotide sequence set forth in SEQ ID NO:5, wherein the nucleic acid molecule encodes a MMP-25 polypeptide that exhibits catalytic activity that is the same as that of a wild-type MMP-25 polypeptide comprising the amino acid sequence set forth in SEQ ID NO:6. Applicants further submit that amended claim 1 particularly points out that the claimed nucleic acid molecule comprises a nucleotide sequence that is 85% identical to the full-length sequence, which is the sequence set forth in SEQ ID NO:5. The cited GenBank document discloses a sequence that is less than 50% identical to SEQ ID NO:1, less than 30% identical to

SEQ ID NO:3, and less than 25% identical to SEQ ID NO:5. Therefore, AA424347 fails to teach or suggest the subject matter of the instant claims.

Applicants respectfully submit that the presently claimed invention meets the novelty requirements under 35 U.S.C. § 102 and request that these rejections be withdrawn.

REJECTION UNDER 35 U.S.C. § 103

The PTO rejects claims 3-7 under 35 U.S.C. § 103, alleging that the claims are obvious over GenBank Acc. No. AA424347 in view of Robison. The PTO concedes that AA424347 does not teach a method of hybridization using the sequences disclosed therein, nor does it teach vectors or host cells comprising such sequences. The PTO asserts, however, that Robison generally teaches PCR and hybridization and teaches vectors and host cells comprising nucleic acids. The PTO alleges that a person having ordinary skill in the art would use the teachings of Robison to produce the protein encoded by AA424347 to analyze its function and would use hybridization to identify nucleic acids that correspond to the sequence disclosed in AA424347.

Applicants respectfully traverse this rejection and submit that the documents cited by the Action, alone or in combination, fail to teach or suggest the subject matter of the instant claims. Applicants respectfully submit that the PTO has not established a *prima facie* case of obviousness. (*See In re Mayne*, 104 F.3d 133, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.)). The PTO must show (1) that the combined references teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, something in the prior art as a whole must suggest the desirability, thus the obviousness, of making the combination. (*In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

Applicants respectfully submit that AA424347 alone or in combination with Robison fails to teach or suggest all the limitations of the present claims. Furthermore, and as discussed above, the present invention was complete prior to the effective filing date (March 26, 1999) of the Robison patent, thus Robison is not a prior art document under 35 U.S.C. § 102 (see Declaration under 37 C.F.R. § 1.131 submitted herewith).

Even if Robison were a prior art document under 35 U.S.C. § 102, its general disclosures of vectors, host cells, and hybridization techniques would not remedy the deficiencies of AA424347. As discussed above, AA424347 fails to teach or suggest an isolated nucleic acid molecule that consists of a nucleotide sequence set forth in SEQ ID NO:1, or an isolated nucleic acid molecule that comprises a nucleotide sequence set forth in SEQ ID NO:3 or SEQ ID NO:5. The cited document also fails to teach or suggest a nucleic acid molecule that shares at least 85% identity with SEQ ID NO:5, wherein the nucleic acid molecule encodes a MMP-25 polypeptide that exhibits catalytic activity that is the same as that of the wild-type MMP-25 polypeptide (SEQ ID NO:6). The EST disclosed in AA424347 is less than 50% identical to SEQ ID NO:1, less than 30% identical to SEQ ID NO:3, and less than 25% identical to SEQ ID NO:5. AA424347 also fails to teach or suggest a method of identifying a nucleic acid molecule encoding all or a part of a MMP-25 polypeptide, wherein the method comprises hybridizing a nucleic acid molecule sample to an oligonucleotide encoding a peptide consisting of an amino acid sequence at positions 1-61, 98-111, or 161-170 of SEQ ID NO:6; and identifying a sequence in the nucleic acid sample that hybridizes to the oligonucleotide under high stringency conditions. The EST disclosed in AA424347 shares identity with a portion of SEQ ID NO:5 beginning at position 741, which corresponds to amino acid position 243; therefore, the cited document does not disclose a nucleotide sequence of an oligonucleotide recited in the claimed hybridization method.

Furthermore, a person having ordinary skill in the art could not reasonably expect to achieve Applicants' invention successfully by preparing a vector that would contain the EST sequence disclosed in AA424347 when the EST has only 411 nucleotides that are contained in SEQ ID NO:1 (833 nucleotides), SEQ ID NO:3 (1488 nucleotides), or SEQ ID NO:5 (1841 nucleotides). The EST shares identity with a portion of SEQ ID NO:1 (nucleotides 1-411) that

encodes SEQ ID NO:2, a portion of SEQ ID NO:3 (653-1063) that encodes SEQ ID NO:4, and a a portion of SEQ ID NO:5 (741-1151) that encodes SEQ ID NO:6; therefore, insertion of the EST sequence into a vector and expression of the EST in a host cell would not be expected to produce the polypeptides encoded by the presently claimed nucleic acid molecules. Accordingly, Applicants submit that the PTO has failed to establish a *prima facie* case of obviousness.

Applicants respectfully submit that the presently claimed invention is nonobvious, satisfying the requirements under 35 U.S.C. § 103. Applicants therefore respectfully request that this rejection be withdrawn.

Applicants respectfully submit that all claims remaining in the Application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Kai Wang et al.

SEED Intellectual Property Law Group PLLC

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Enclosure:

Declaration under 37 C.F.R. §1.131
Copy of Invention Disclosure Form
Copy of Consent to Assignment of and Agreement to Amend Invention and Proprietary Information Agreement

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